Basics on Developing Source Data Collection Tools and Case Report Forms for Clinical Research Studies

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Conflict of Interest

The presenters do not have any financial or personal conflict of interest to report in relation to this presentation.

RPN Workshop “Mini-series” on Research Documentation and Data Collection

February:

Basics on Developing Source Data Collection tools and Case Report Forms for Clinical Research Studies

March:

Basics on REDCap: A Tool for Data Collection (Topic, title to come)

April:

Advanced REDCap: Techniques on Creating REDCap forms (Topic, title to come)

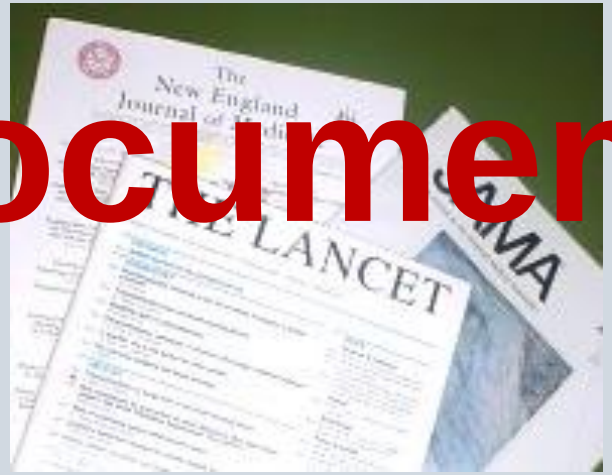
Objectives

- Review basics on study documentation and importance of adequate study documentation in clinical/human research;
- Define relevant terms: Source data, Source documentation, Data Collection tools, Checklists, Case Report Forms, ALCOA-C;
- Demonstrate how to develop study documents to ensure adherence to ALCOA-C and documentation best practices;
- Demonstrate basics on how to develop Case Report Forms (CRFs) for your study.

DATA is the product of your study …..

Your study data supports the study hypothesis ….

Your Documentation!



You publish articles in medical journals on the basis of your data …..

Your data contributes to changing practice …..

What supports your data?

Your data…..

Your documentation…..

CERTIFICATE OF GOLD VALIDATION

This gold nugget has undergone extensive expert examination and testing and it is officially determined that this gold nugget is in fact REAL GOLD!

What affects Data quality?

Study design:

- What questions are asked
- How we define what data will be collected
- Data Sources

Processes:

- How we collect the data
- How we record the data
- How we “support” the data (metadata)
- How we monitor the data
- Training and qualifications of study staff

Systems to capture/store data:

- Audit trail
- Security – who can access the data

Study Documentation – Regulations and Guidance

OHRP/ Common Rule 45 CFR 46	"Informed consent shall be documented by the use of a written informed consent form approved by the IRB and signed (including in an electronic format) by the subject or the subject's legally authorized representative." (45 CFR 46.117)
FDA 21 CFR 312	" An investigator is required to prepare and maintain **adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual** administered drug or employed as a control in the investigation…. Case histories **include the case report forms AND *supporting* data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital chart(s), and the nurses' notes.** The case history for each individual shall document that informed consent was obtained prior to participation in the study. (21 CFR 312.62(b))
ICH GCP E6(R2) Good Clinical Practice: Integrated Addendum to ICH E6(R1), March, 2018	"The investigator/institution should **maintain adequate and accurate source documents and trial records that include all pertinent observations on each of the site's trial subjects. Source data should be attributable, legible, contemporaneous, original, accurate, and complete.** Changes to source data should be traceable, should not obscure the original entry, and should be explained if necessary (e.g., via an audit trail)." (ICH GCP 4.9.1) "Essential documents are those documents that individually and collectively permit evaluation of the conduct of a trial and the quality of the data produced …. serve to demonstrate **compliance of the investigator, sponsor, and monitor with the standards of GCP and all applicable regulatory requirements**." (ICH GCP 8.1)

Documentation – Common Terms

Source Data	All information in original records and certified copies of original records of **clinical findings, observations, or other activities in a clinical trial necessary for reconstruction and evaluation of the trial**. Source data is contained in source documents." *(ICH GCP 1.51)* ○ Source must meet ALCOA-C standard
Source Documents (including source data collection forms)	The original record that contains the source data (EMR, research data collection form, lab report, REDCap survey completed by subjects, informed consent form, study progress notes, etc.). - Data generated by researcher should be attributable (signed and dated).

Documentation – Common Terms

Case Report Form (CRF/eCRF)	Protocol specific document created as a data collection/transmission tool ○ Can be paper or electronic (for purposes of this presentation we will be referring to electronic case report forms) ○ Provides a way to record study data in a clear logical consistent manner. ○ Should only capture data that is specified in the approved protocol. **If source data is entered directly onto the CRF, then the CRF is considered a source document.** That source data should be attributable (signed/dated). ○ Use of CRFs as source documents should be specified in the study protocol, per ICH GCP 6.4.9.
Data Collection Forms/Tools/ Worksheets, etc.	Tool used by/created by the site to show that the procedures of the study visit were conducted as per protocol ○ Typically more data is recorded than in a Case Report Form *(explanation further on)* • For example, if recording source data, that source data should be attributable to the person who generated the data (signature/initials and date)
Checklists	Tool that can be used to document/verify that study procedures were completed (including documentation to support they were done). ○ NOT necessarily source data/documents! If parts of checklists serve as source data collection that data must meet ALCOA-C standard (to be discussed further, but this would include signature/initials and date)

Documentation – Common Terms

REDCap (Research Electronic Data Capture)	A software system (developed by Vanderbilt University) in 2004 to enable clinical researchers to create research databases in a secure, HIPAA-compliant system. REDCap allows users great flexibility and functionality in creating and managing web-based data collection systems. It is capable of compliance with HIPAA and FDA Part 11 requirements.
Electronic Data Capture (EDC)	Software/website for electronically capturing data via case report forms
Clinical Trial Management System (CTMS)	Software/website often used by CROs to manage a clinical trial ▪ Can include an EDC, but also includes additional modules and tools used to manage project management aspects of a clinical trial

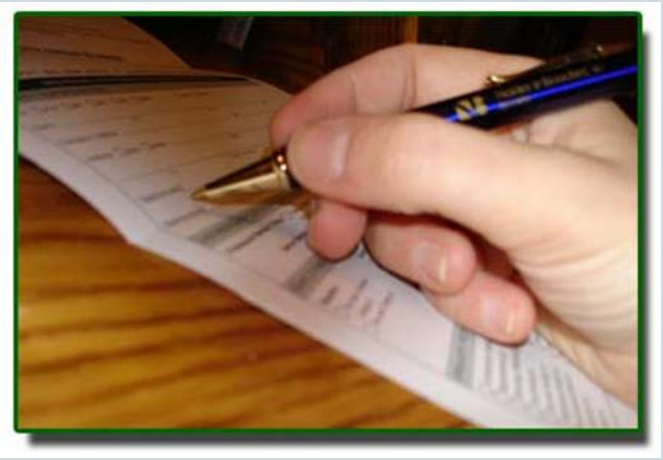
Study Documentation – Purpose

- Documents the existence of subjects
- Record of clinical decisions/opinions
- Demonstrates compliance with the protocol and regulations
- Shows study was conducted appropriately
- Enables reconstruction of study ("audit trail")
- Shows appropriate oversight of the investigator
- **Substantiate the integrity of trial data collected**
- **Give confidence that the data is valid and reliable**

"…Someone is going to deconstruct that sausage…. Where is it hanging together and where is it not?..." FDA Scientist

CRFs – Purpose

- Demonstrates compliance with the study protocol and statistical analysis plan
- Facilitates complete and standardized data collection within and across sites
- Promotes efficient processing, analysis, and reporting of study information
- Enables exchange of data across sites to the Sponsor/trial PI/Data Coordinating Center, etc.
- Ensures proper conduct of the trial
- Preserves and maintains the quality and integrity of the data



Functionality of eCRFs

- Real time feedback to sites regarding data errors
- Real time monitoring of study data
- Real time feedback to sites regarding protocol procedures
- Facilitates standardization of data capture across sites

Source Data – two main categories

1) Exists (or will exist) independent of/outside of the research
   - Ex: Medical or school records

Source document is that record

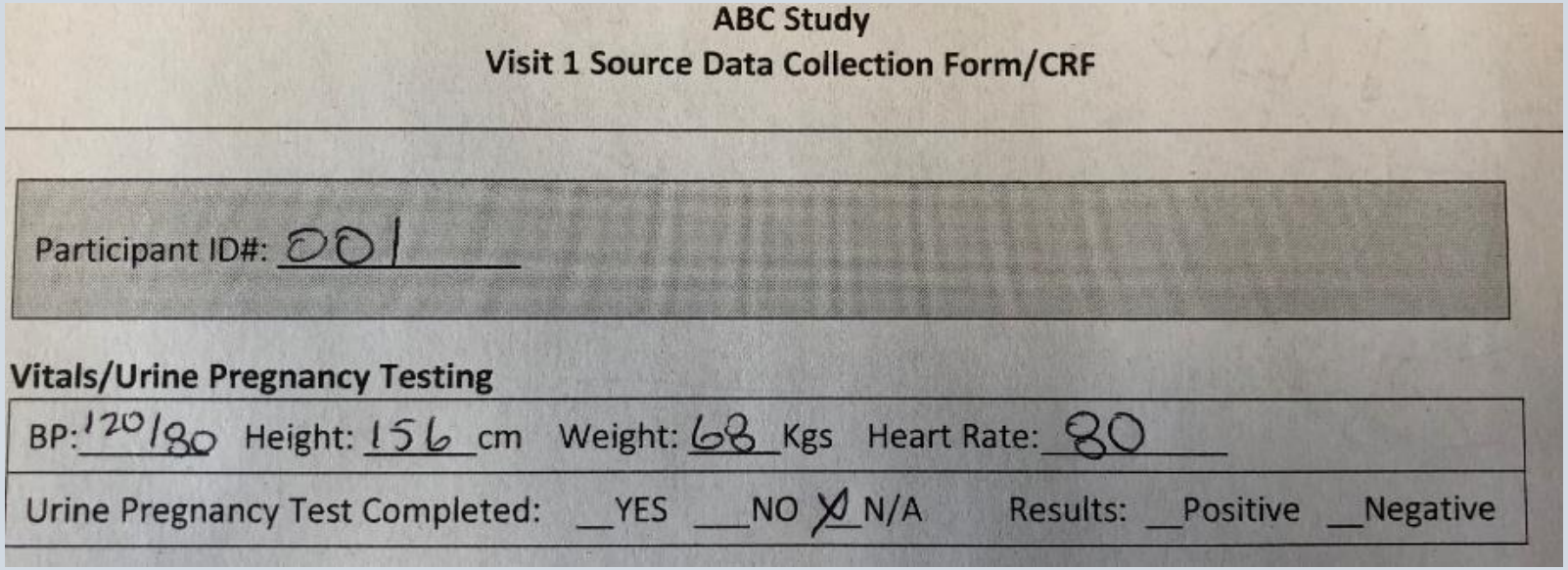
2) Generated through procedures/measures/assessments that are part of the research
   - Vital signs and physical exam done specifically for research purposes
   - Assessments done specifically for research purposes
     - assessments of AEs
     - assessments of efficacy of intervention, etc.
     - data provided by subjects via questionnaires or surveys

Source document is where the study team or subject records the data (could be paper or electronic form)

ALCOA-C Documentation Standards

Attributable	- Data should be linked to its source - Who observed and recorded the data and traceable to the source of the data itself - Applies to changes made to the data (i.e. need signature/date) - "All data entries shall be dated on the date of entry and signed or initialed by the person entering the data."
Legible	- Capable of being read - Changes don't obscure original entry - Signatures should be legible
Contemporaneous	- The data, signature, and date need to be completed at the same time/as close to the event as possible - Prompt data collection with respect to time of observation → better quality - "All data entries shall be dated on the date of entry…".
Original	- First and most accurate, reliable recording of the information (paper, electronic) - "Data shall be recorded directly…"
Accurate	- Free from error, consistent, real representation of facts, the truth - Conforming to a standard (i.e. protocol) - Errors have been identified and corrected with notes to explain if needed
Complete	- Study documentation must be complete

Attributable?



ABC Study
Visit 1 Source Data Collection Form/CRF

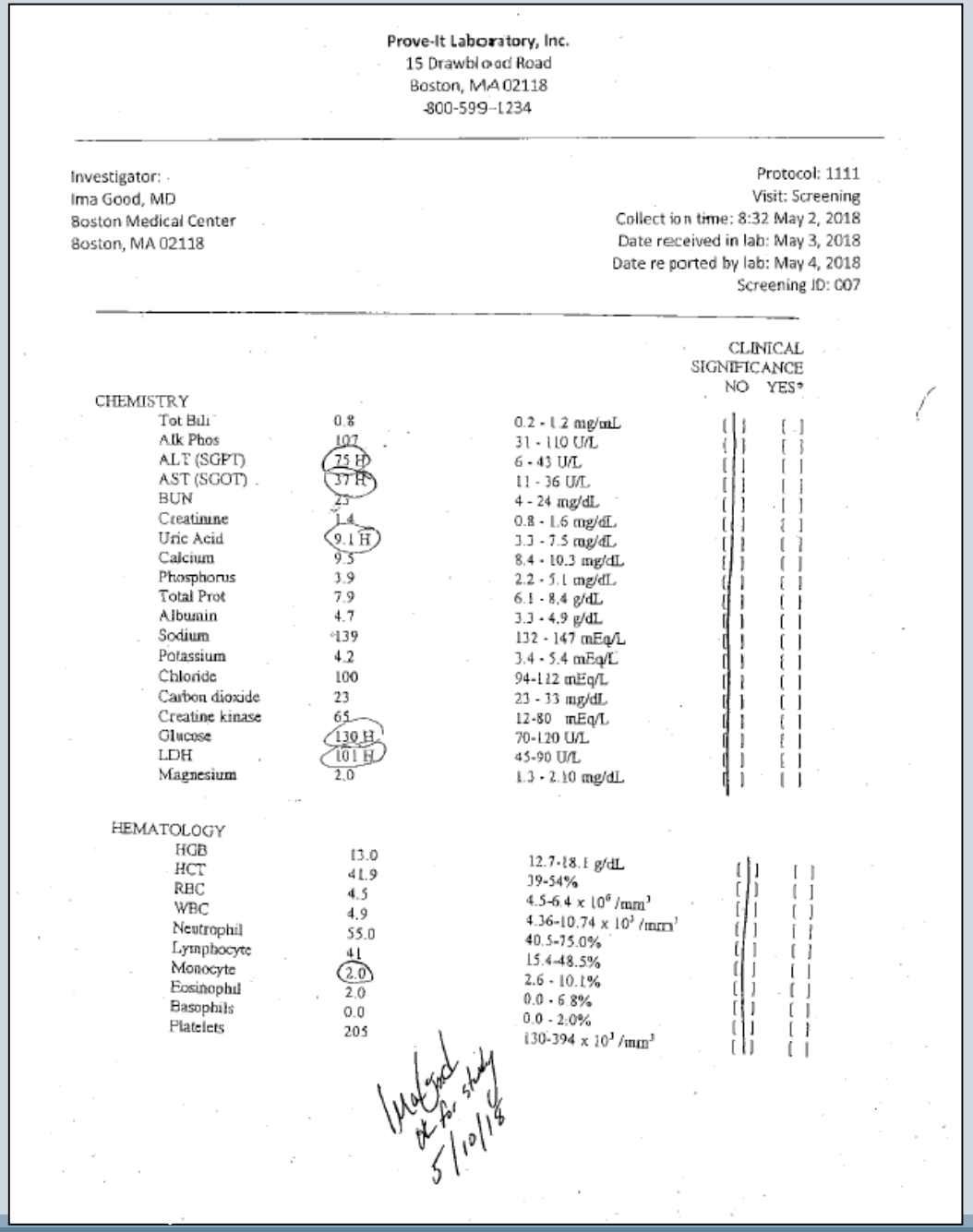
Participant ID#: 001

Vitals/Urine Pregnancy Testing

BP: 120/80 Height: 156 cm Weight: 68 Kgs Heart Rate: 80

Urine Pregnancy Test Completed: __YES ___NO X N/A Results: __Positive __Negative

Attributable?



Prove-It Laboratory, Inc.
15 Drawblood Road
Boston, MA 02118
800-599-1234

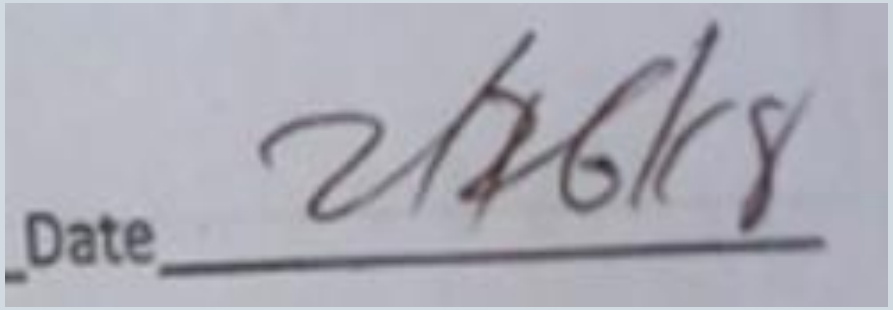
Investigator:
Ima Good, MD
Boston Medical Center
Boston, MA 02118

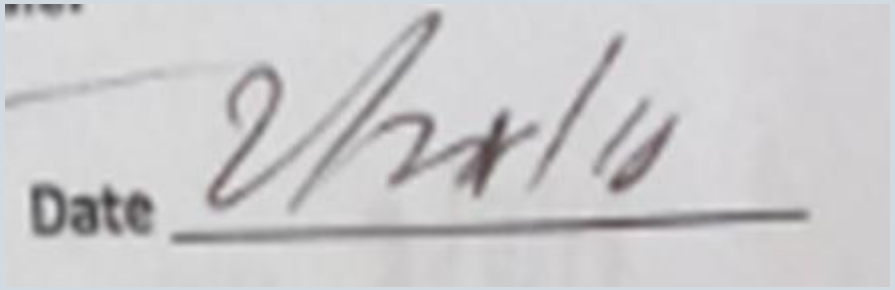
Protocol: 1111
Visit: Screening
Collection time: 8:32 May 2, 2018
Date received in lab: May 3, 2018
Date reported by lab: May 4, 2018
Screening ID: 007

			CLINICAL SIGNIFICANCE NO	YES*
CHEMISTRY				
Tot Bili	0.8	0.2 - 1.2 mg/mL	[ ]	[ ]
Alk Phos	107	31 - 110 U/L	[ ]	[ ]
ALT (SGPT)	75 H	6 - 43 U/L	[ ]	[ ]
AST (SGOT)	37 H	11 - 36 U/L	[ ]	[ ]
BUN	23	4 - 24 mg/dL	[ ]	[ ]
Creatinine	1.4	0.8 - 1.6 mg/dL	[ ]	[ ]
Uric Acid	9.1 H	3.3 - 7.5 mg/dL	[ ]	[ ]
Calcium	9.5	8.4 - 10.3 mg/dL	[ ]	[ ]
Phosphorus	3.9	2.2 - 5.1 mg/dL	[ ]	[ ]
Total Prot	7.9	6.1 - 8.4 g/dL	[ ]	[ ]
Albumin	4.7	3.3 - 4.9 g/dL	[ ]	[ ]
Sodium	139	132 - 147 mEq/L	[ ]	[ ]
Potassium	4.2	3.4 - 5.4 mEq/L	[ ]	[ ]
Chloride	100	94-112 mEq/L	[ ]	[ ]
Carbon dioxide	23	23 - 33 mg/dL	[ ]	[ ]
Creatine kinase	65	12-80 mEq/L	[ ]	[ ]
Glucose	130 H	70-120 U/L	[ ]	[ ]
LDH	101 H	45-90 U/L	[ ]	[ ]
Magnesium	2.0	1.3 - 2.10 mg/dL	[ ]	[ ]
HEMATOLOGY				
HGB	13.0	12.7-18.1 g/dL	[ ]	[ ]
HCT	41.9	39-54%	[ ]	[ ]
RBC	4.5	4.5-6.4 x 10^6 /mm^3	[ ]	[ ]
WBC	4.9	4.36-10.74 x 10^3 /mm^3	[ ]	[ ]
Neutrophil	55.0	40.5-75.0%	[ ]	[ ]
Lymphocyte	41	15.4-48.5%	[ ]	[ ]
Monocyte	2.0	2.6 - 10.1%	[ ]	[ ]
Eosinophil	2.0	0.0 - 6.8%	[ ]	[ ]
Basophils	0.0	0.0 - 2.0%	[ ]	[ ]
Platelets	205	130-394 x 10^3 /mm^3	[ ]	[ ]

Ima Good
OK for study
5/10/18

Legible?

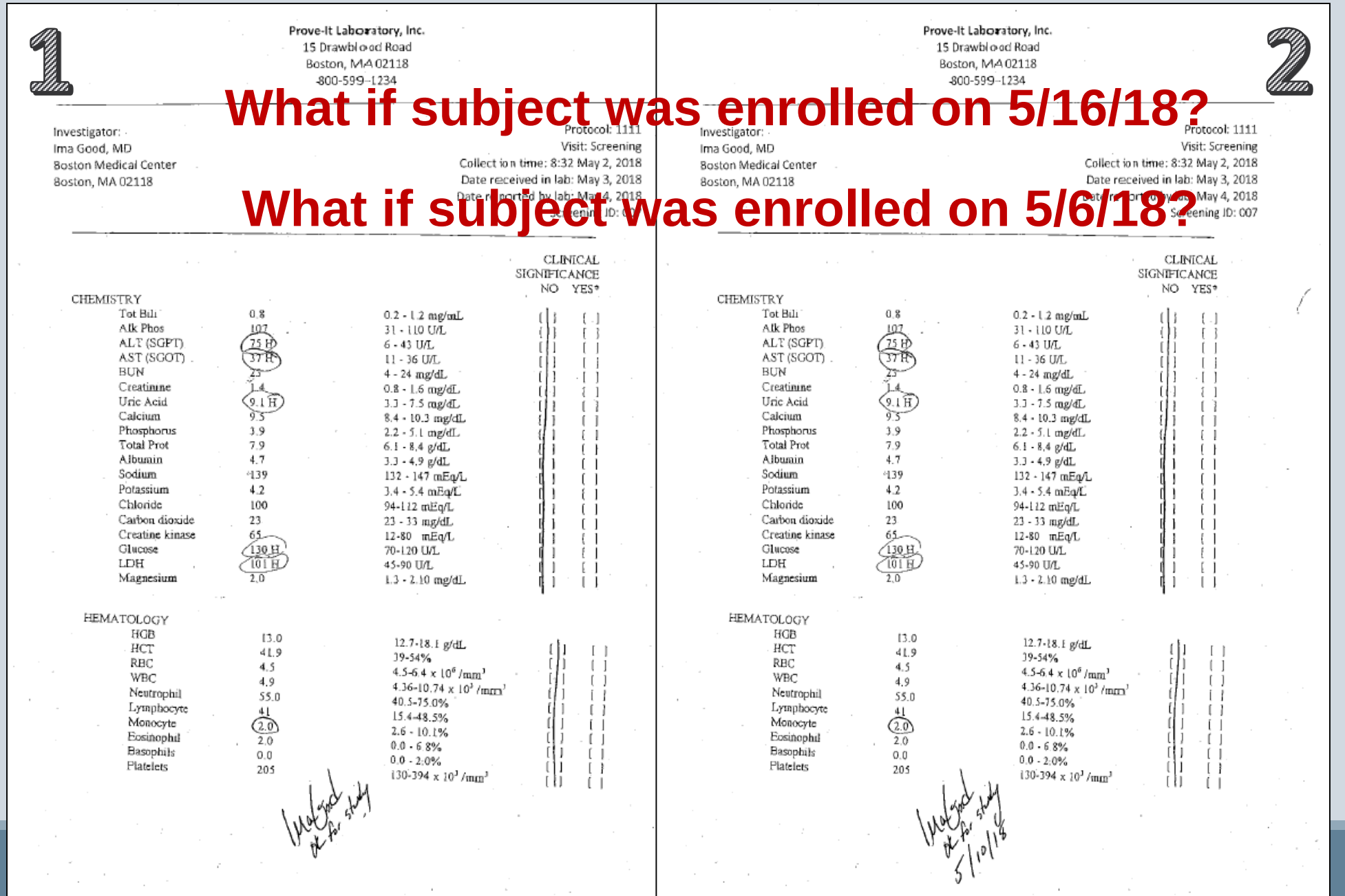




Contemporaneous?

What if subject was enrolled on 5/16/18?

What if subject was enrolled on 5/6/18?



1

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Protocol ok for study

2

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Protocol ok for study 5/10/18

Original?

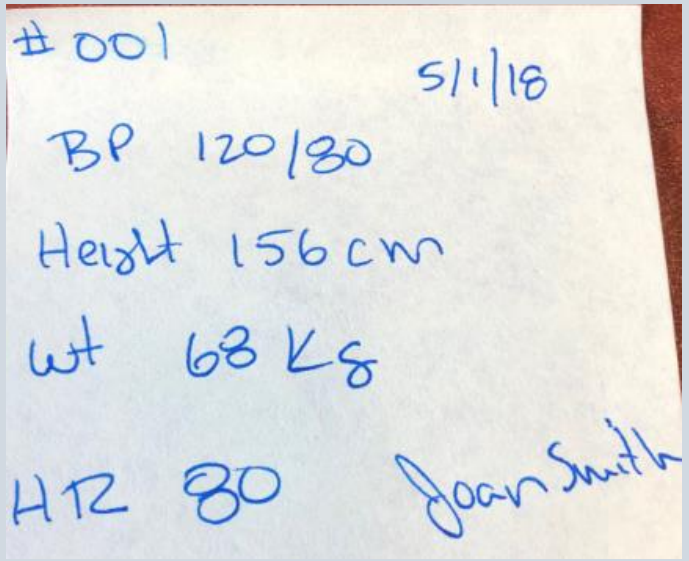
ABC Study
Visit 1 Source Data Collection Form/CRF

Participant ID#: 001

Vitals/Urine Pregnancy Testing

BP: 120/80 Height: 156 cm Weight: 68 Kgs Heart Rate: 80

Urine Pregnancy Test Completed: __YES ___NO X N/A Results: __Positive __Negative



Accurate?

- Study coordinator didn't have access to a Snellen chart, so estimated the subject vision without testing required by the protocol.
- Subject temperature taken after subject had a cup of coffee and temperature of 99.9 F was recorded.
- The PI made assumptions about pregnancy status for teen subjects without doing the testing specified in the protocol.

Complete?

Date: 02/10/2022 (mm/dd/yyyy)

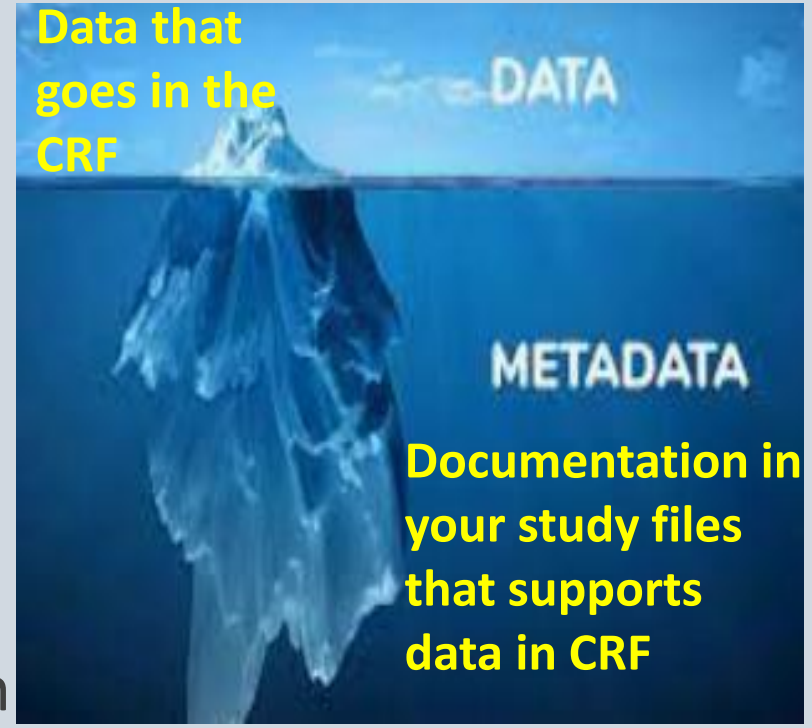
Subject ID: 001-1

SMOKING HISTORY		
☐ Non smoker		
☐ Smoker, date started	___/_____ (mmm/yyyy)	Duration: __ __ years
☒ Ex-smoker, Date stopped:	MAR/2014 (mmm/yyyy)	Duration: __ __ years

Sign: [signature] Date: 2/10/22

Metadata/Supporting data *(i.e. your documentation)*

- **Data *about* the data**….
- FDA term: "Supporting data…." *(21 CFR 312.62)*
- Gives meaning to the data ….TELLS THE STORY of your data
- **Who, what, when, where, why?**
- Audit trail
  - Shows details for: creation, modification, deletion of records
- Assures us we have quality data and we can rely on the data to answer the study questions!



Data point entered into eCRF (along with date collected and subject ID)

142/83

Extra info recorded on Data collection form:

Jane Smith, RN (would be signature or initials)

2/14/2022

If it was a trial on hypertension, there may be some other "supporting data" that would be needed:

- Sitting, lying, standing
- Time BP taken and # times
- Machine vs. not
- Validating appropriate cuff size used

Study Documentation:
An Inspection Example

FDA Warning letter: You failed to prepare and maintain adequate and accurate case histories… (Edward Mostei, 5/16/08)

The protocol excluded patients with a calculated serum creatinine clearance <30mL/min, as determined by the Cockcroft Gault formula…. Of 50 subjects whose records were audited, source records failed to document the calculated serum creatinine clearance value for all 50 subjects… exclusion of subjects with creatinine clearance <30mL/min is crucial to ensure the safety of subjects with renal impairment. Your response letter… states that this value was calculated, but not documented.

Your explanation is unacceptable. Without documentation, there is no way to verify that subjects were eligible for enrollment into the study, as determined by calculated serum creatinine clearance…"

Data collection	Data point	Metadata (Supporting data) examples
Adverse event in COVID inpatient clinical trial	**Moderate LFT elevations (AST & ALT)**	▪ When did the event happen? ▪ When was the study team aware? ▪ Who from the study team assessed the event (seriousness, severity/grade, expectedness, relatedness) ○ Related regulatory documentation should show: were they trained, delegated, qualified, IRB-approved? ▪ When was it assessed? ▪ Details on reporting (if applicable)

What is the **Source Document** in each column?

	1	2	3	4	5
A	Source Data: Elig. screening question responses	Source Data: Vital signs taken at research visit	Source Data: Adverse Events from EMR (elec. medical record)	Source Data: Mini-Mental Exam from EMR	Source Data: Weekly participant questionnaire responses
B	Recorded on a hardcopy data collection form	Recorded on a hardcopy data collection form	Recorded on hardcopy data collection form	Recorded on hardcopy data collection form	
C	Entered on a hardcopy CRF		Study MD documents assessments on hardcopy data collection form		
D	eCRF/Study database	eCRF/Study database	eCRF/Study database	eCRF/Study database	Entered in REDCap by RA (eCRF/Study database)

Checklist

- A tool to help ensure that all procedures/assessments for a study visit have been completed.
- **Careful….Is your checklist a source document?**

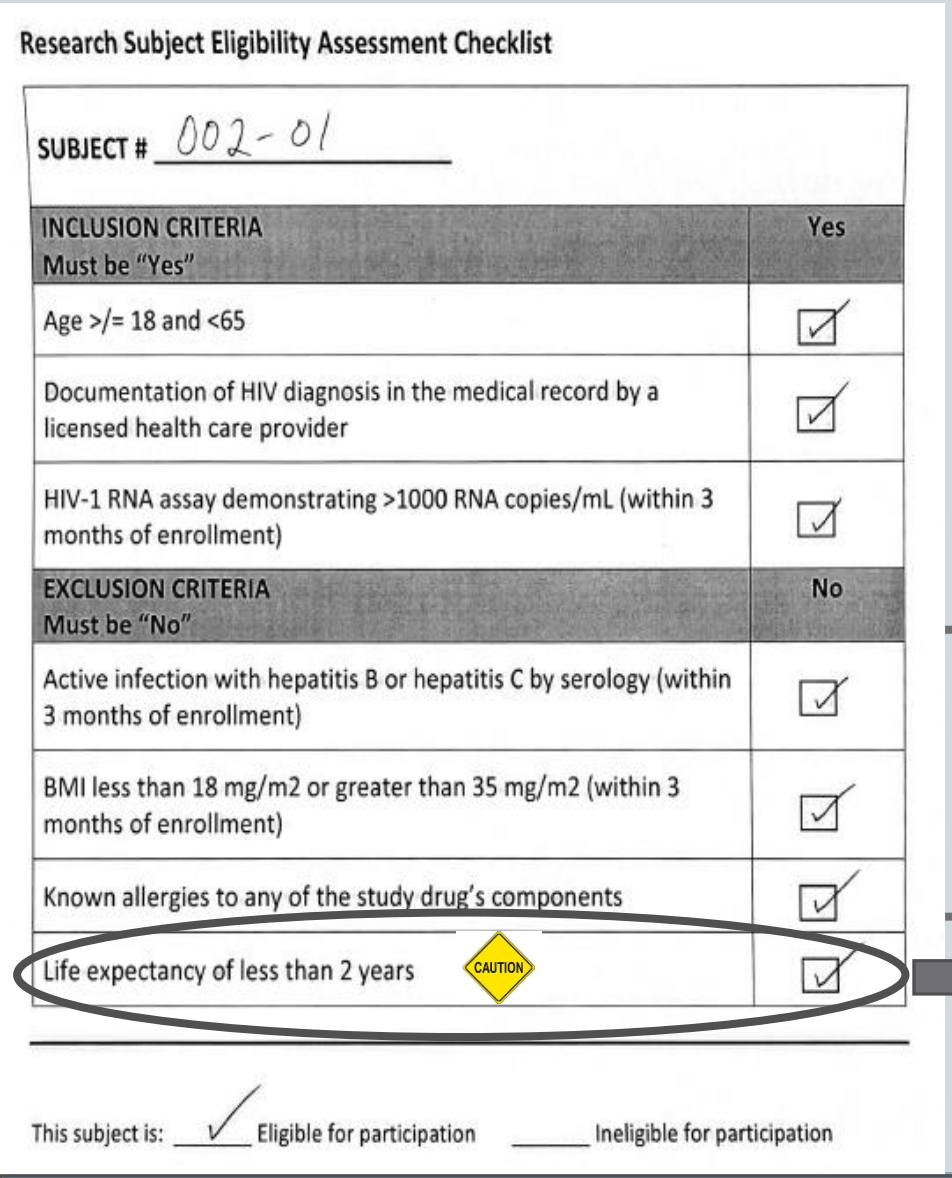
- Hint:
  - Is it first entry of any *study data*?
  - Are you using it as a “sign-off” by the PI/investigator that the subject meets criteria?

ABC Study
Visit 1 Checklist

Participant #:_____ Date of Visit:_____

Procedure/Assessment	Completed
Inclusion/Exclusion Assessment	☐
Blood Labs collected and sent to lab	☐
Participant Randomized	☐
Participant Provided Study Drug and Diary	☐
Participant Reimbursement Payment/Clin Card	☐
Study Visit Data Updated eCRF	☐

Example: Checklist that is also Source documentation



Research Subject Eligibility Assessment Checklist

SUBJECT # 002-01

INCLUSION CRITERIA Must be "Yes"	Yes
Age >/= 18 and <65	☑
Documentation of HIV diagnosis in the medical record by a licensed health care provider	☑
HIV-1 RNA assay demonstrating >1000 RNA copies/mL (within 3 months of enrollment)	☑
EXCLUSION CRITERIA Must be "No"	**No**
Active infection with hepatitis B or hepatitis C by serology (within 3 months of enrollment)	☑
BMI less than 18 mg/m2 or greater than 35 mg/m2 (within 3 months of enrollment)	☑
Known allergies to any of the study drug's components	☑
Life expectancy of less than 2 years CAUTION	☑

This subject is: ✓ Eligible for participation _____ Ineligible for participation

Source documents: medical record/study labs

Source documents: medical record/study labs

What is needed here?

What source data/documentation is needed to validate each eligibility criterion?

Inclusion:

- Age >/=18 and <65
- Documentation of HIV diagnosis in the medical record by a licensed health care provider;
- HIV-1 RNA assay demonstrating >1000 RNA copies/mL

Exclusion:

- Active infection with hepatitis B or hepatitis C by serology
- BMI less than 18 mg/m2 or greater than 35 mg/m2
- Known allergies to any of the study drug's components
- Life expectancy of less than 2 years

Example of Eligibility checklist that notes location of source data

[Link to form]

RESEARCH SUBJECT ELIGIBILITY ASSESSMENT FORM

CRRO Template Version 1.0, 4/25/2017

GENERAL INSTRUCTIONS – delete this box from the completed form

NOTE: This form is designed to be a starting point on eligibility assessment. Update it as necessary for your specific study.

All participants enrolled in the study must meet all inclusion criteria and not meet any of the exclusion criteria. All changes to inclusion/exclusion criteria must be approved by the IRB prior to implementation. Remember to modify this template any time the inclusion/exclusion criteria is changed.

Participant records should include source documentation (lab results, medical records, questionnaires, data collection tools, etc.) to support that the participant meets eligibility criteria.

All staff responsible for reviewing and/or determining subject eligibility should be listed on the IRB application, appropriately trained by study PI, and listed on the study delegation log.

Red text represents instructions to you – to be deleted from the final version.

Study Name:	
IRB Protocol #:	
Protocol Version # and/or Date:	
Principal Investigator:	

[Complete this table with all inclusion/exclusion criteria listed in the IRB-approved protocol. Modify the number of rows as needed depending on the number of inclusion/exclusion criteria in your protocol.]

SUBJECT # _____

INCLUSION CRITERIA *Must be "yes"*	Yes	No	Location of supporting source documentation	Notes
1.	☐	☐		
2.	☐	☐		
3.	☐	☐		
4.	☐	☐		
5.	☐	☐		

EXCLUSION CRITERIA *Must be "no"*	Yes	No	Location of supporting source documentation	Notes
1.	☐	☐		
2.	☐	☐		
3.	☐	☐		
4.	☐	☐		
5.	☐	☐		

This subject is:

☐ Eligible for participation ☐ Ineligible for participation

[Signed by study team member who is (1) qualified to assess eligibility and (2) delegated this study task by the PI]

Signature:	Date:
Printed Name:	

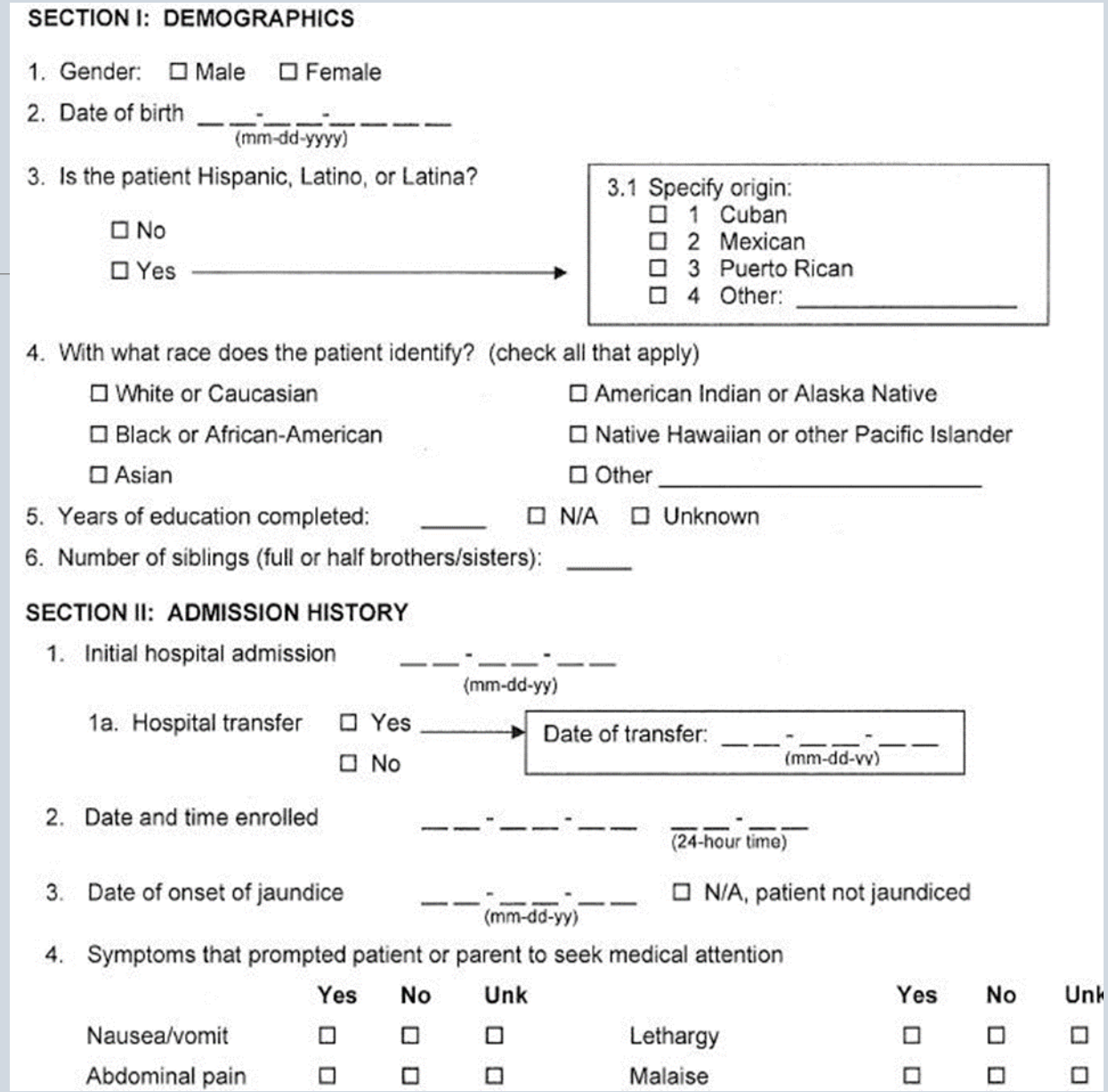
Research Subject Eligibility Assessment Form
CRRO Template Version 1.0, 4/25/2017

The Basics of CRF Design

- Standard structure
- Ease of data entry
- Accommodate the person collecting the data
  - Consider the workload!
- All data points should be related
- Only data points to be collected at a particular time point should be on one form
- Ask simple questions
- Evident units
- No duplication
- Answer options must be exhaustive and mutually exclusive
- Use skip pattern controls
- Use standards, if available
- Version control
- Consider if the CRF may be used as a source document

Poor CRF Design

- Questions jump around the page
- Boxes used for all answer options, whether select one or check all that apply
- Questions are not uniquely numbered
- Questions can be interpreted differently
- Missing units
- No version control



SECTION I: DEMOGRAPHICS

1. Gender: ☐ Male ☐ Female
2. Date of birth __ __-__ __-__ __ __ __ (mm-dd-yyyy)
3. Is the patient Hispanic, Latino, or Latina?
   - ☐ No
   - ☐ Yes → 3.1 Specify origin:
     - ☐ 1 Cuban
     - ☐ 2 Mexican
     - ☐ 3 Puerto Rican
     - ☐ 4 Other: _____
4. With what race does the patient identify? (check all that apply)
   - ☐ White or Caucasian
   - ☐ Black or African-American
   - ☐ Asian
   - ☐ American Indian or Alaska Native
   - ☐ Native Hawaiian or other Pacific Islander
   - ☐ Other _____
5. Years of education completed: _____ ☐ N/A ☐ Unknown
6. Number of siblings (full or half brothers/sisters): _____

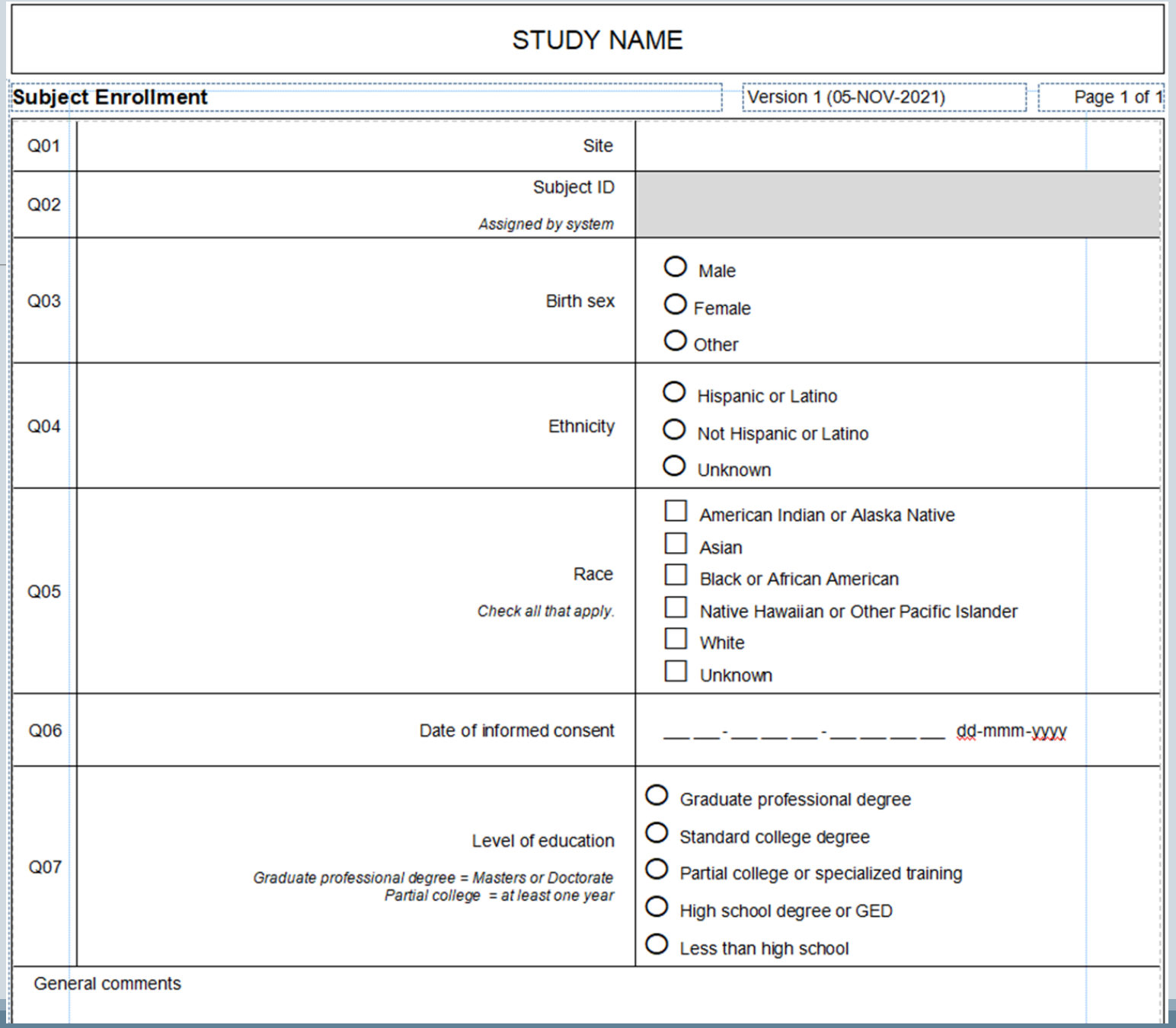
SECTION II: ADMISSION HISTORY

1. Initial hospital admission __ __-__ __-__ __ (mm-dd-yy)
   - 1a. Hospital transfer ☐ Yes → Date of transfer: __ __-__ __-__ __ (mm-dd-yy)
   - ☐ No
2. Date and time enrolled __ __-__ __-__ __ __ __-__ __ (24-hour time)
3. Date of onset of jaundice __ __-__ __-__ __ (mm-dd-yy) ☐ N/A, patient not jaundiced
4. Symptoms that prompted patient or parent to seek medical attention

	Yes	No	Unk		Yes	No	Unk
Nausea/vomit	☐	☐	☐	Lethargy	☐	☐	☐
Abdominal pain	☐	☐	☐	Malaise	☐	☐	☐

Good CRF Design

- Questions are listed clearly
- Radio buttons used for selecting one answer option and check boxes for check all that apply
- Questions are uniquely numbered
- Minimize questions being interpreted differently by modifying answer options and adding instructions
- Units indicated (date)
- Version control



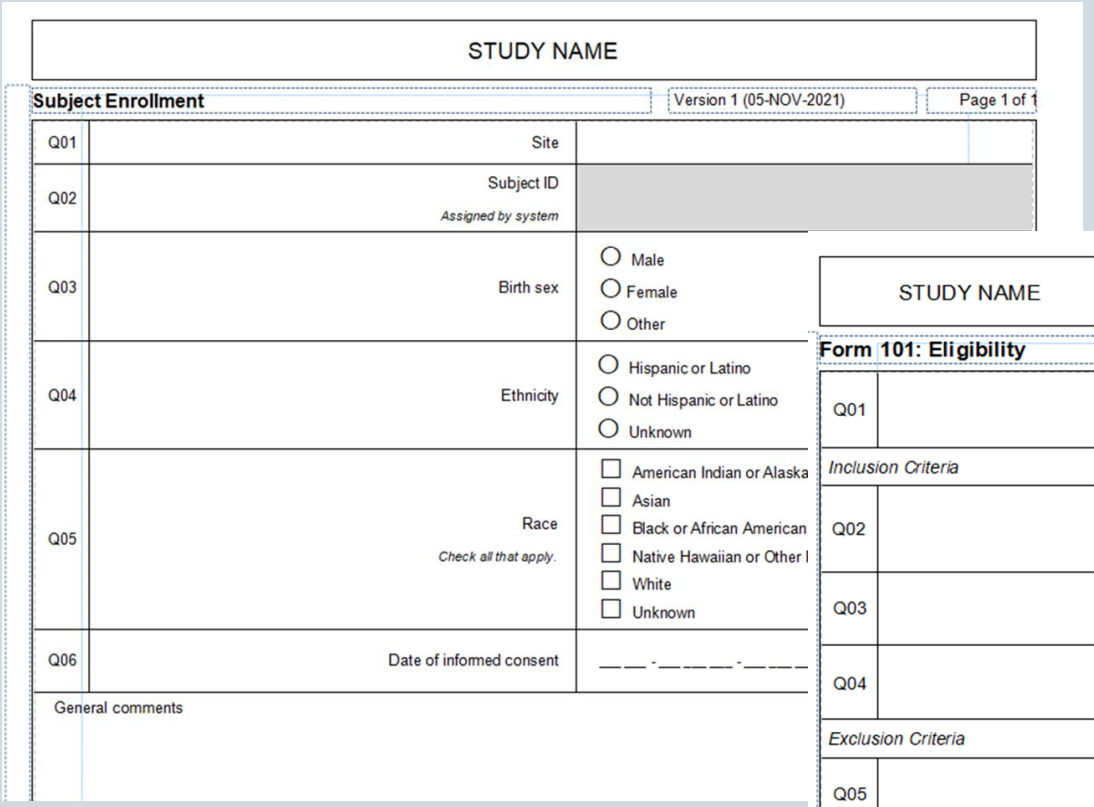
STUDY NAME

Subject Enrollment | Version 1 (05-NOV-2021) | Page 1 of 1

Q01	Site	
Q02	Subject ID *Assigned by system*	
Q03	Birth sex	○ Male ○ Female ○ Other
Q04	Ethnicity	○ Hispanic or Latino ○ Not Hispanic or Latino ○ Unknown
Q05	Race *Check all that apply.*	☐ American Indian or Alaska Native ☐ Asian ☐ Black or African American ☐ Native Hawaiian or Other Pacific Islander ☐ White ☐ Unknown
Q06	Date of informed consent	__ __-__ __ __-__ __ __ __ dd-mmm-yyyy
Q07	Level of education *Graduate professional degree = Masters or Doctorate* *Partial college = at least one year*	○ Graduate professional degree ○ Standard college degree ○ Partial college or specialized training ○ High school degree or GED ○ Less than high school

General comments

Standard Structure

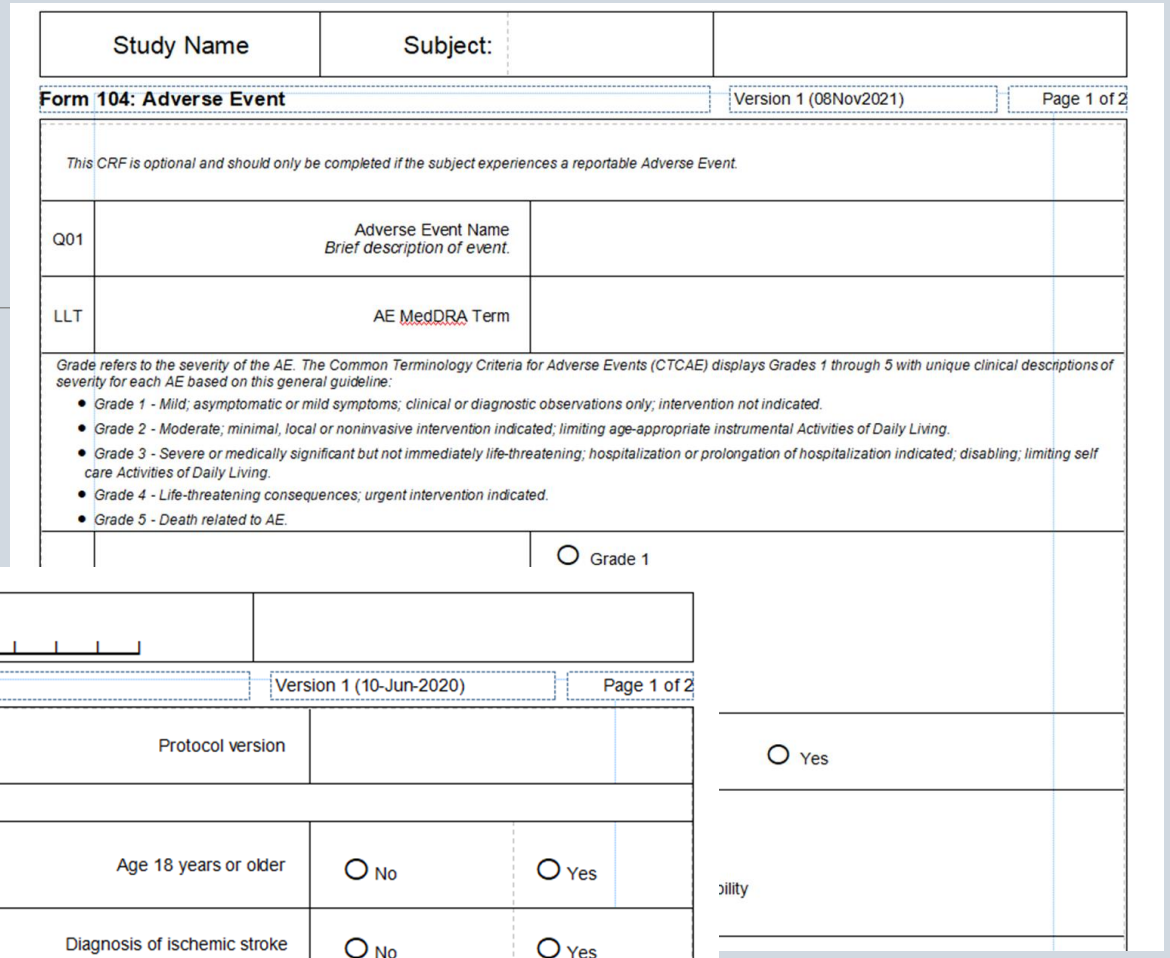


STUDY NAME

Subject Enrollment | Version 1 (05-NOV-2021) | Page 1 of 1

Q01	Site	
Q02	Subject ID *Assigned by system*	
Q03	Birth sex	○ Male ○ Female ○ Other
Q04	Ethnicity	○ Hispanic or Latino ○ Not Hispanic or Latino ○ Unknown
Q05	Race *Check all that apply.*	☐ American Indian or Alaska ☐ Asian ☐ Black or African American ☐ Native Hawaiian or Other I ☐ White ☐ Unknown
Q06	Date of informed consent	__ __ - __ __ __ - __ __ __ __

General comments



Study Name | Subject:

Form 104: Adverse Event | Version 1 (08Nov2021) | Page 1 of 2

This CRF is optional and should only be completed if the subject experiences a reportable Adverse Event.

Q01	Adverse Event Name *Brief description of event.*	
LLT	AE MedDRA Term	

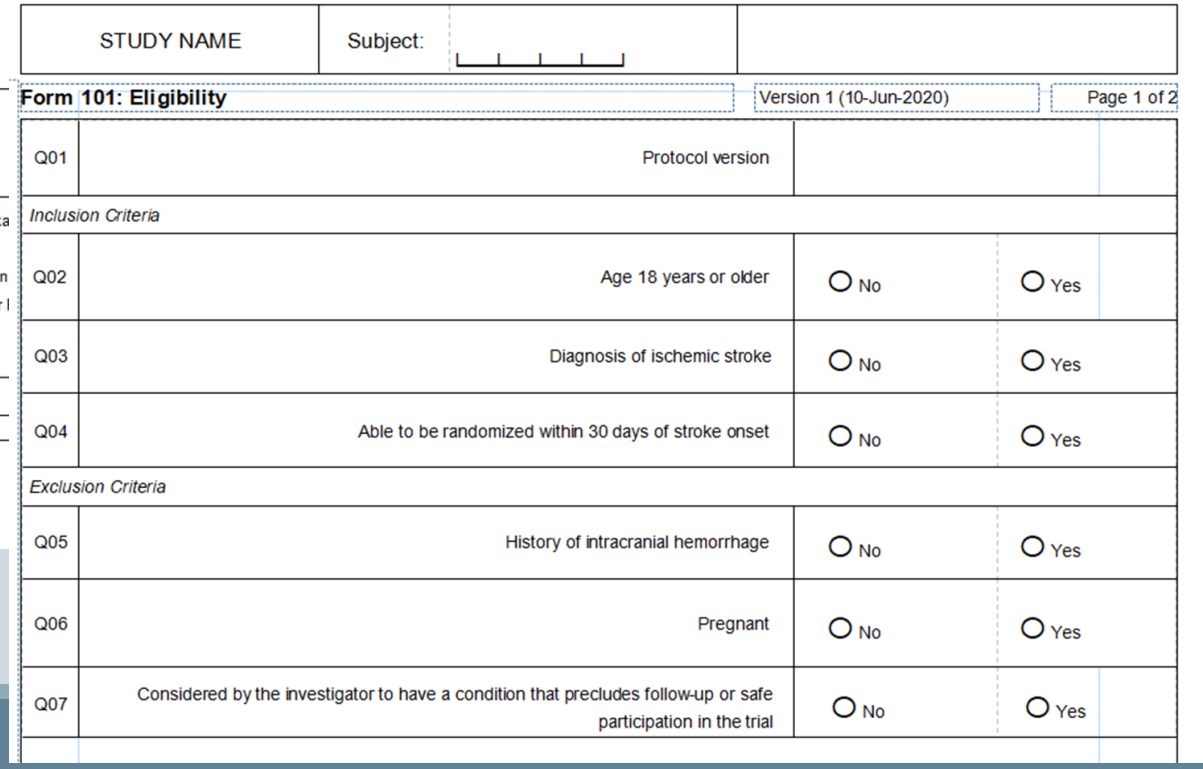
Grade refers to the severity of the AE. The Common Terminology Criteria for Adverse Events (CTCAE) displays Grades 1 through 5 with unique clinical descriptions of severity for each AE based on this general guideline:

- *Grade 1 - Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated.*
- *Grade 2 - Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental Activities of Daily Living.*
- *Grade 3 - Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self care Activities of Daily Living.*
- *Grade 4 - Life-threatening consequences; urgent intervention indicated.*
- *Grade 5 - Death related to AE.*

○ Grade 1

○ Yes

ility



STUDY NAME | Subject: ____

Form 101: Eligibility | Version 1 (10-Jun-2020) | Page 1 of 2

Q01	Protocol version		
Inclusion Criteria			
Q02	Age 18 years or older	○ No	○ Yes
Q03	Diagnosis of ischemic stroke	○ No	○ Yes
Q04	Able to be randomized within 30 days of stroke onset	○ No	○ Yes
Exclusion Criteria			
Q05	History of intracranial hemorrhage	○ No	○ Yes
Q06	Pregnant	○ No	○ Yes
Q07	Considered by the investigator to have a condition that precludes follow-up or safe participation in the trial	○ No	○ Yes

Ask Simple Questions

Q01: Baseline blood glucose < 50mg/dL or > 400mg/dL? Yes / No

Q01: Baseline blood glucose is _____ (mg/dl)

Q02: How long since your last dentist visit? _____ (days)

Q02: Date of your last dentist visit: _ _/ _ _ / _ _ _ _ (mm/dd/yyyy)

Q03: Did the patient have chickenpox or measles in the past 12 months and ear infection in the past 6 month? Yes / No

Q03: Did the patient had chickenpox in the past 12 months? Yes/No
Q04: Did the patient had measles in the past 12 months? Yes/No
Q05: Did the patient had ear infection in the past 6 months? Yes/No

Answer Options

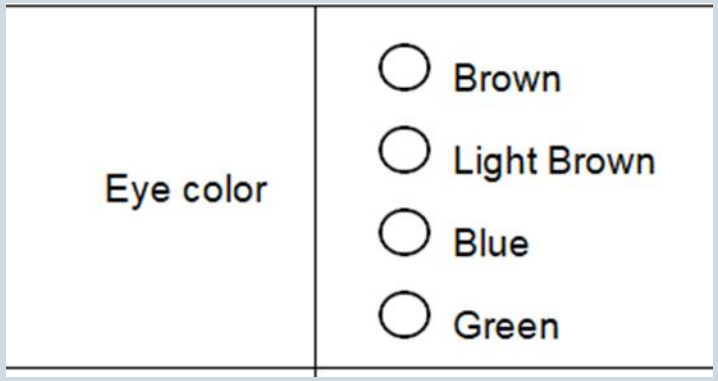
Check all that Apply **vs** ***Select One***

Race *Check all that apply.*	☐ American Indian or Alaska Native ☐ Asian ☐ Black or African American ☐ Native Hawaiian or Other Pacific Islander ☐ White ☐ Unknown

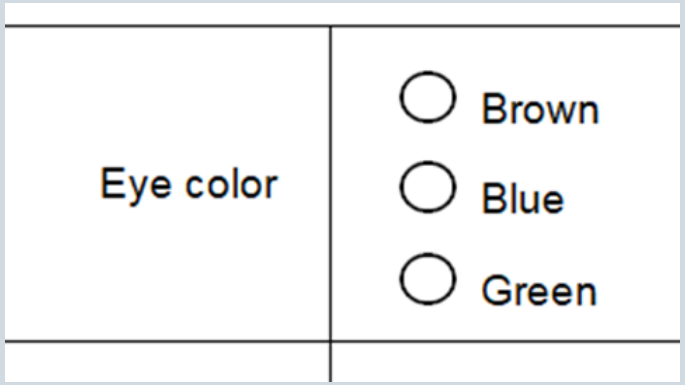
Primary reason for study termination	○ Study completed ○ Death ○ Lost to follow-up ○ Consent withdrawn ○ Other

Answer Options must be Mutually Exclusive…

Bad Example

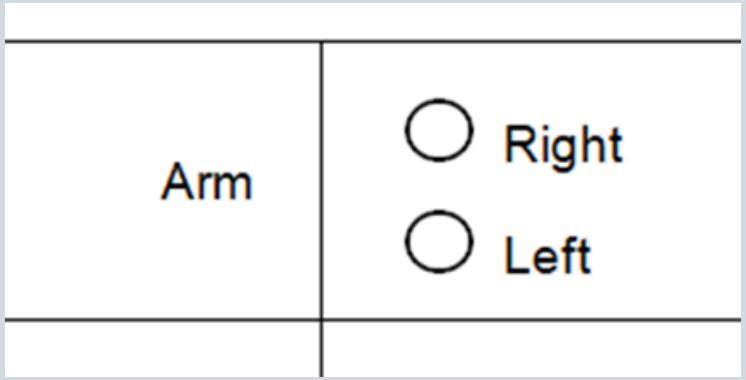


Good Example

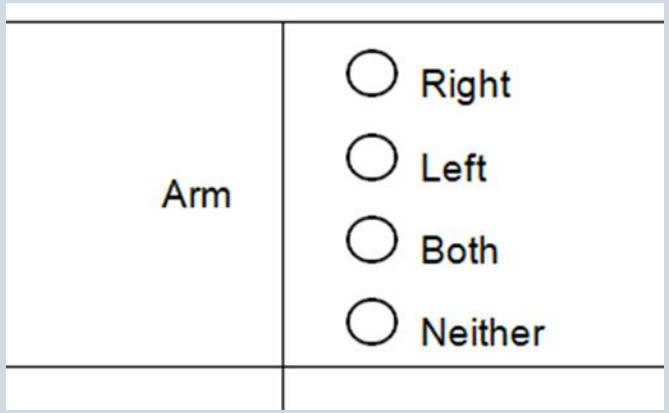


…And Exhaustive

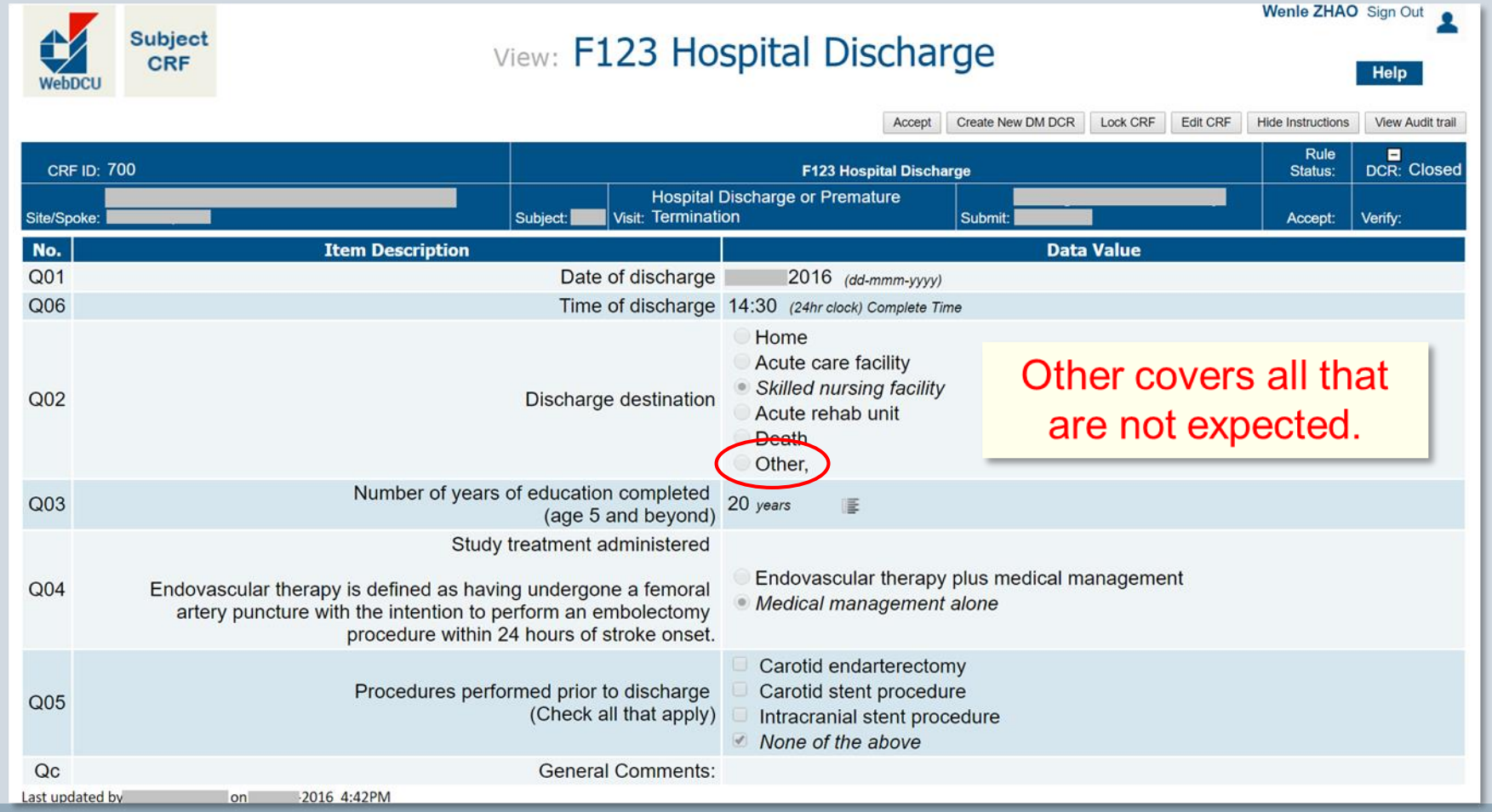
Bad Example



Good Example



Consider all possible responses!



WebDCU Subject CRF

Wenle ZHAO Sign Out

View: F123 Hospital Discharge

Help

Accept | Create New DM DCR | Lock CRF | Edit CRF | Hide Instructions | View Audit trail

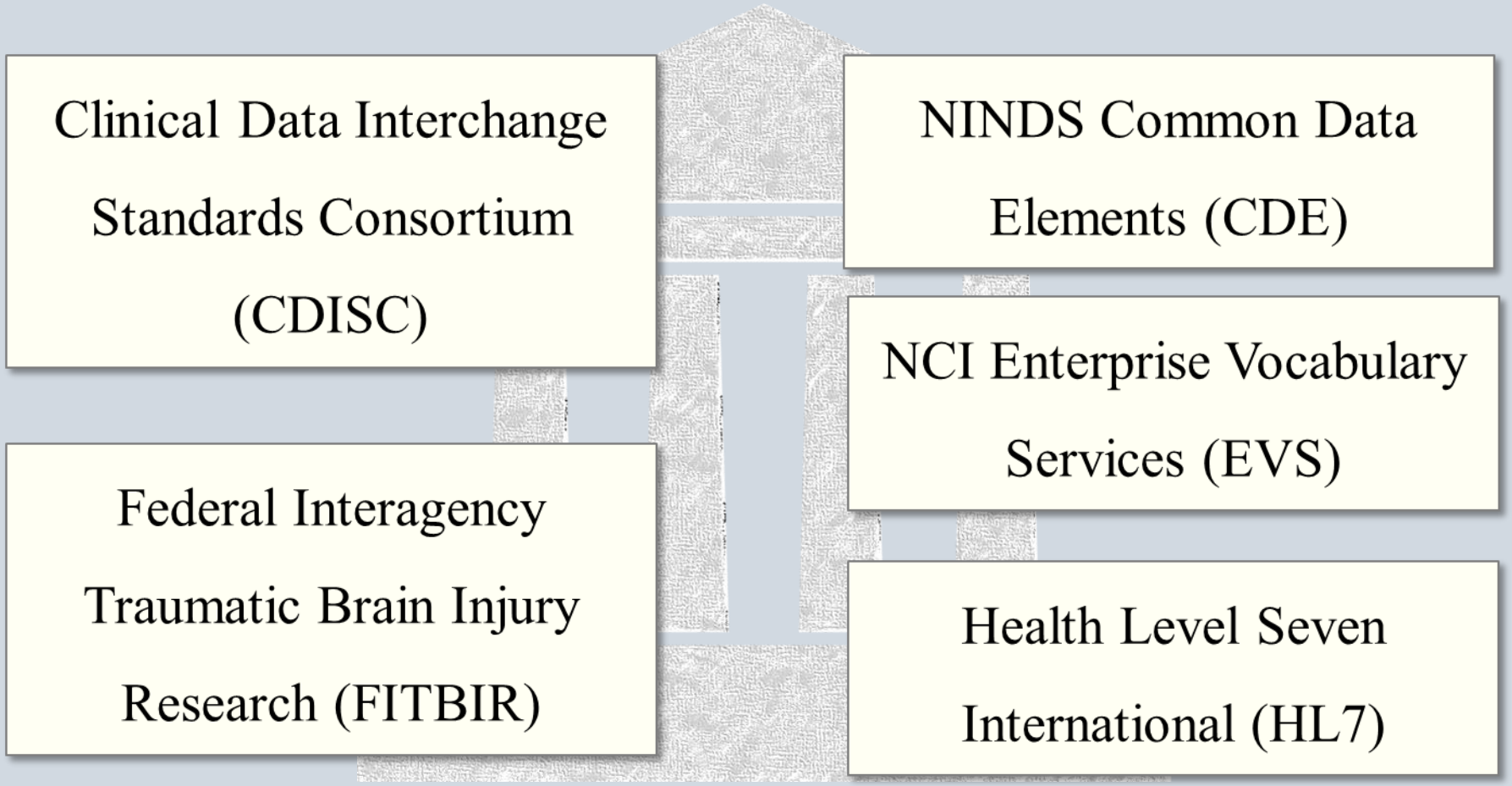
CRF ID: 700	F123 Hospital Discharge			Rule Status:	DCR: Closed
Site/Spoke: [redacted]	Subject: [redacted]	Visit: Hospital Discharge or Premature Termination	Submit: [redacted]	Accept:	Verify:

No.	Item Description	Data Value
Q01	Date of discharge	[redacted]2016 *(dd-mmm-yyyy)*
Q06	Time of discharge	14:30 *(24hr clock) Complete Time*
Q02	Discharge destination	○ Home ○ Acute care facility ◉ *Skilled nursing facility* ○ Acute rehab unit ○ Death ○ Other,
Q03	Number of years of education completed (age 5 and beyond)	20 *years*
Q04	Study treatment administered Endovascular therapy is defined as having undergone a femoral artery puncture with the intention to perform an embolectomy procedure within 24 hours of stroke onset.	○ Endovascular therapy plus medical management ◉ *Medical management alone*
Q05	Procedures performed prior to discharge (Check all that apply)	☐ Carotid endarterectomy ☐ Carotid stent procedure ☐ Intracranial stent procedure ☑ *None of the above*
Qc	General Comments:	

Last updated by [redacted] on [redacted]2016 4:42PM

Other covers all that are not expected.

Use of Standard Coding



Validated Assessments

- Use validated assessments with version and source information to ensure data validity and intellectual property protection
- Examples:
  - Hamilton Rating Scale for Depression (HRS-D)
  - NIH Stroke Scale (NIHSS)
  - The Short Form (36) Health Survey (SF-36)
  - Modified Rankin Scale (mRS)
  - Clinical Global Impression (CGI)
  - Glasgow Outcome Scale (GOS)
  - Montgomery-Asberg Depression Rating Scale (MADRS)
  - Quality of Life in Neurological Disorders (Neuro-QOL)
  - Pediatric Stroke Outcome Measure Short Neuro Exam (PSOM-SNE)
  - King's Outcome Scale for Childhood Head Injury (KOSCHI)

When to start drafting CRFs?

- The BEST time to start drafting CRFs is when there is a final draft or initial version of the protocol, but plenty of time before study enrollment starts!
- The following also needs to be considered:
  - Changes will likely be made to the protocol when drafting your CRFs
    - So either wait to submit your final protocol to the IRB or know you will have a protocol amendment prior to starting enrollment
  - When do you anticipate starting enrollment?
    - Estimate how long it will take to develop and program CRFs
  - What other processes need to be discussed and finalized?
    - Examples: Study drug, Central lab, Safety monitoring and reporting, etc.

Where to Start?

Step 1: Read the protocol and make notes on anything relevant to your electronic data capture system.

- Compare study overview, study procedures, and table of assessments/events if available.
- Identify trial's primary, secondary, and tertiary outcomes and determine what data will need to be collected for these
- Note any discrepancies and follow up with the clinical team

Step 2: Draft a CRF collection schedule

- Define your study visits and what forms will need to be collected at each visit

Step 3: Use your draft CRF Collection Schedule to identify what CRFs are needed.

- Sketch out and start drafting CRFs.

Step 4: If you have standard or common form templates, use them!

- Enrollment demographics, Medical History, Adverse event, Con Med Log, End of Study
- Validated assessments

Step 5: Draft study-specific forms

- You will need the guidance of the clinical study team for these!

Schedule of Events → CRF Collection Schedule

Table 1: Schedule of Events

	Baseline	Treatment	30 days post treatment
Informed Consent	X		
History & Physical	X		
Quality of Life Scale	X		X
Physical Exam	X	X	X
CT scan	X		X
CBC with platelets	X		X
Vital signs	X	X	X
Study Treatment		X	
Assess for adverse events		X	X

CRF Collection Schedule

Form #	Form Name	Baseline	Treatment	30 Days Post Treatment	End of Study
101	Subject Enrollment	X			
102	Eligibility	X			
103	Randomization	X			
104	Adverse Event	OR	OR	OR	
105	Labs	X		X	
106	Medical History	X			
107	Quality of Life Scale	X		X	
108	Imaging	X		X	
109	Vital Signs	X	X	X	
110	Study Drug Administration		X		
111	End of Study				X

X = Required; O = Optional; R = Repeatable

Important Reminders when Developing CRFs!

- Make sure you collect the data needed to answer the study question
- Only collect the data you are IRB-approved to collect
- Less is more! The more data you collect, the more data the sites have to enter and you have to monitor and clean.
- Simplify questions and answers and instead add instructions when necessary

Planning for Missing Data

- Allow sites to indicate on CRF if data is missing
  - Enter a specific code if info is missing (e.g. 9999)
  - Pop-up to alert site
  - Have site enter reason if missing
- If possible, have system flag any fields that were accidentally missed
- Use skip patterns
  - If Q01 is yes, then Q02 must be answered
- If system allows, add database rules to check for missing data, data out of range, or incorrect date/time sequences.
  - This can cut down on data entry errors!
  - Rules can be programmed within one CRF or across CRFs

There are so many ways to walk the dog ☺

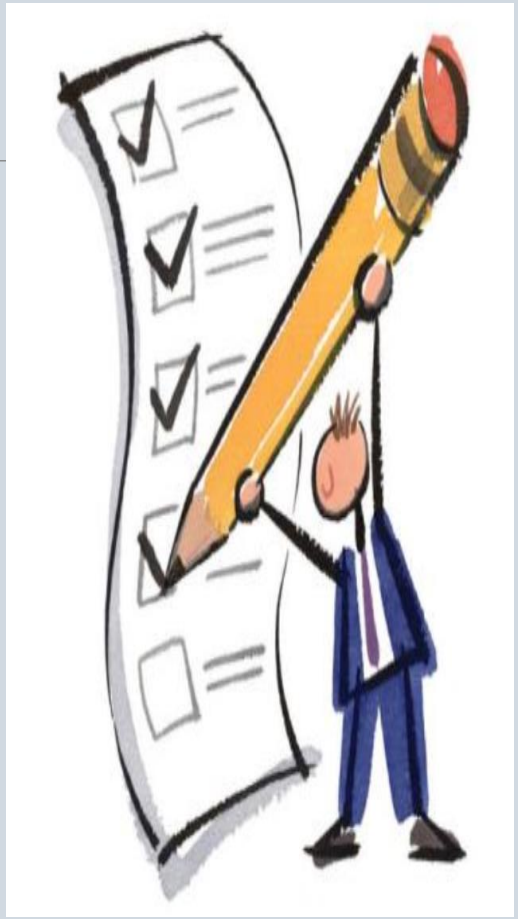
- **Keep in mind as you develop your data collection…**
  - Where is your source data going to exist?
  - Paper? Electronic? Both?
  - Either way, make sure the source data/documentation adheres to ALCOA-C

    Who, When, etc.

This should be determined before building/creating data collection tools (including CRFs)

Creating Source Data Collection Forms

- Paper or electronic or combo
  - If electronic, use a system like REDCap that maintains an audit trial (don't use an Excel spreadsheet to capture source!)
- Keep in mind purpose of the source: verify that the data collected is valid…. Follow ALCOA-C
- Review protocol and develop forms around the data collection needs for each visit…mapping protocol to data collection.



Creating Source Data Collection Forms

- Include items for:

Date (time if necessary)	Place to record who collected/generated the data and when
Subject ID	Maybe include source of the data (if from medical record)
Visit # or visit name	Version number/date of form
Space to record values for procedures/ assessments	Format of values

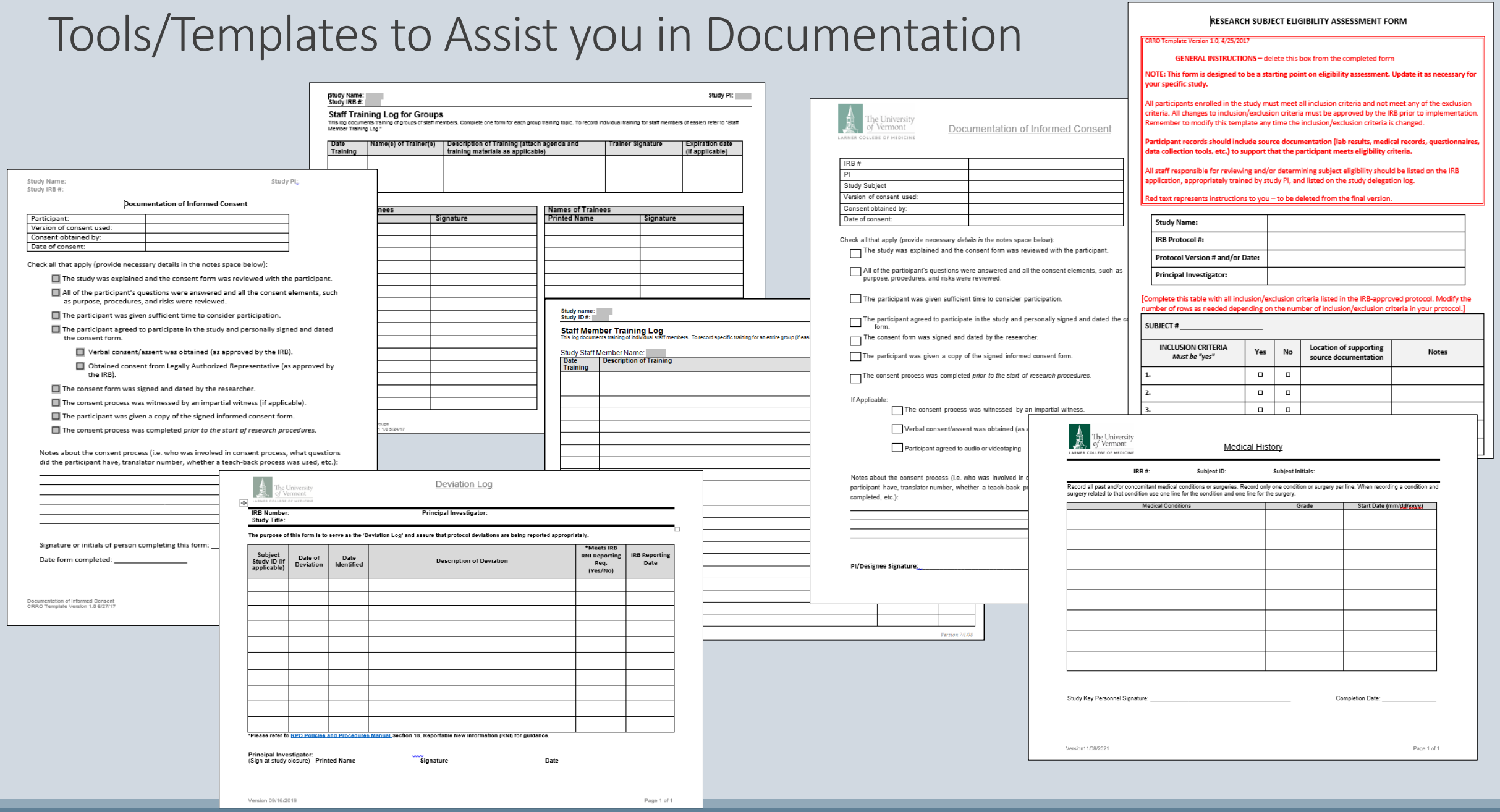
A few additional considerations on developing source data collection forms

- Progress notes are helpful! They help to "tell the story," especially for more complicated studies. Use of progress notes can also decrease the **need for endless Notes to File (NTFs).**
- Informed consent: Your source documentation of informed consent can be as simple as the signed and dated consent form (which is a source document). However, additional documentation may be necessary, depending on the consent scenario.
  - For example: Some HRPPs require involvement of a Licensed Independent Provider (LIP) for greater than minimal risk drug and device clinical trials. If the LIP does not sign the consent, but is involved in the consent process this should be described somewhere (and that will also be a source document). You can implement a consent progress note for this (or a general progress note).

A few additional considerations on developing source data collection forms

- Make sure that you carefully review the protocol for specific data collection requirements.
  - For example: study required that an assessment score be “Obtained in person at by a certified investigator at baseline.” However in practice the team simply used the assessment score that was done per standard care.
- Remember that printouts of the sponsor-supplied CRFs are not necessarily the forms you should use as your source documentation. They are often not designed to meet ALCOA-C (because they are not intended to be source documents). What are the “metadata” that is needed in addition?

Tools/Templates to Assist you in Documentation



Study Name:
Study IRB #:
Study PI:

Staff Training Log for Groups

This log documents training of groups of staff members. Complete one form for each group training topic. To record individual training for staff members (if easier) refer to "Staff Member Training Log."

Date Training	Name(s) of Trainer(s)	Description of Training (attach agenda and training materials as applicable)	Trainer Signature	Expiration date (if applicable)

Names of Trainees	
Printed Name	Signature

Study Name:
Study IRB #:
Study PI:

Documentation of Informed Consent

Participant:	
Version of consent used:	
Consent obtained by:	
Date of consent:	

Check all that apply (provide necessary details in the notes space below):

- The study was explained and the consent form was reviewed with the participant.
- All of the participant's questions were answered and all the consent elements, such as purpose, procedures, and risks were reviewed.
- The participant was given sufficient time to consider participation.
- The participant agreed to participate in the study and personally signed and dated the consent form.
  - Verbal consent/assent was obtained (as approved by the IRB).
  - Obtained consent from Legally Authorized Representative (as approved by the IRB).
- The consent form was signed and dated by the researcher.
- The consent process was witnessed by an impartial witness (if applicable).
- The participant was given a copy of the signed informed consent form.
- The consent process was completed *prior to the start of research procedures.*

Notes about the consent process (i.e. who was involved in consent process, what questions did the participant have, translator number, whether a teach-back process was used, etc.):

Signature or initials of person completing this form:

Date form completed:

Documentation of Informed Consent
CRRO Template Version 1.0 6/27/17

Study name:
Study ID #:

Staff Member Training Log

This log documents training of individual staff members. To record specific training for an entire group (if eas

Study Staff Member Name:

Date Training	Description of Training

Version 7.1.08

The University of Vermont
LARNER COLLEGE OF MEDICINE

Deviation Log

IRB Number:
Study Title:
Principal Investigator:

The purpose of this form is to serve as the 'Deviation Log' and assure that protocol deviations are being reported appropriately.

Subject Study ID (if applicable)	Date of Deviation	Date Identified	Description of Deviation	*Meets IRB RNI Reporting Req. (Yes/No)	IRB Reporting Date

*Please refer to RPO Policies and Procedures Manual Section 18. Reportable New Information (RNI) for guidance.

Principal Investigator:
(Sign at study closure) Printed Name Signature Date

Version 09/16/2019 Page 1 of 1

The University of Vermont
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Documentation of Informed Consent

IRB #	
PI	
Study Subject	
Version of consent used:	
Consent obtained by:	
Date of consent:	

Check all that apply (provide necessary *details in* the notes space below):

- The study was explained and the consent form was reviewed with the participant.
- All of the participant's questions were answered and all the consent elements, such as purpose, procedures, and risks were reviewed.
- The participant was given sufficient time to consider participation.
- The participant agreed to participate in the study and personally signed and dated the c form.
- The consent form was signed and dated by the researcher.
- The participant was given a copy of the signed informed consent form.
- The consent process was completed *prior to the start of research procedures.*

If Applicable:

- The consent process was witnessed by an impartial witness.
- Verbal consent/assent was obtained (as
- Participant agreed to audio or videotaping

Notes about the consent process (i.e. who was involved in c participant have, translator number, whether a teach-back pr completed, etc.):

PI/Designee Signature:

RESEARCH SUBJECT ELIGIBILITY ASSESSMENT FORM

CRRO Template Version 1.0, 4/25/2017

GENERAL INSTRUCTIONS – delete this box from the completed form

NOTE: This form is designed to be a starting point on eligibility assessment. Update it as necessary for your specific study.

All participants enrolled in the study must meet all inclusion criteria and not meet any of the exclusion criteria. All changes to inclusion/exclusion criteria must be approved by the IRB prior to implementation. Remember to modify this template any time the inclusion/exclusion criteria is changed.

Participant records should include source documentation (lab results, medical records, questionnaires, data collection tools, etc.) to support that the participant meets eligibility criteria.

All staff responsible for reviewing and/or determining subject eligibility should be listed on the IRB application, appropriately trained by study PI, and listed on the study delegation log.

Red text represents instructions to you – to be deleted from the final version.

Study Name:	
IRB Protocol #:	
Protocol Version # and/or Date:	
Principal Investigator:	

[Complete this table with all inclusion/exclusion criteria listed in the IRB-approved protocol. Modify the number of rows as needed depending on the number of inclusion/exclusion criteria in your protocol.]

SUBJECT # _____

INCLUSION CRITERIA *Must be "yes"*	Yes	No	Location of supporting source documentation	Notes
1.	☐	☐		
2.	☐	☐		
3.	☐	☐		

The University of Vermont
LARNER COLLEGE OF MEDICINE

Medical History

IRB #: Subject ID: Subject Initials:

Record all past and/or concomitant medical conditions or surgeries. Record only one condition or surgery per line. When recording a condition and surgery related to that condition use one line for the condition and one line for the surgery.

Medical Conditions	Grade	Start Date (mm/dd/yyyy)

Study Key Personnel Signature: _____ Completion Date: _____

Version11/08/2021 Page 1 of 1

Our Institutional Resources for Study Documentation

UF:

- SOPs, Guidance Documents, and Policies (firewall): https://cancer.ufl.edu/research/clinical-trials-office-2/research-policies-and-helpful-documents/cro-sops-guidance-documents-and-policies/
- Clinical Research Toolkit: https://www.ctsi.ufl.edu/research/research-support/irb-consults/clinical-research-toolkit/

BUMC/BMC:

- Study documentation tools from CRRO: https://www.bumc.bu.edu/crro/tools/

UVM:

- https://commons.med.uvm.edu/dean/comclntril/SitePages/Regulatory%20Documents%20and%20Resources.aspx

MUSC:

- MUSC personnel may submit a SPARCRequest for a Regulatory Consult with the SUCCESS Center for assistance with study documentation.

See Slides and videos from recent RPN Workshop and Clinical Research Seminar

- **RPN Workshop:**

  Electronic Data Capture Systems and Data Management Best Practices

  Annie Penfield-Cyr, MS, UVM, and Jen Holmes, CCRP, UVM

  Jan 25, 2021

  Link: https://www.bumc.bu.edu/crro/research-professional-network/resources-programs/past-rpn-workshops/

- **Clinical Research Seminar:**

  Case Report Form Design

  Kimberly Ann Dukes, PhD, BU SPH

  Nov 17, 2021

  Link: https://www.bumc.bu.edu/crro/training-education/past-seminars/

More resources…

NINDS CRF library: CRF Library | NINDS Common Data Elements (nih.gov)

NINDS CDE library: https://www.commondataelements.ninds.nih.gov/crf-library

NCCIH Clinical Research Toolbox: https://www.nccih.nih.gov/grants/toolbox

NIMH Clinical Research Toolbox: https://www.nimh.nih.gov/funding/clinical-research/clinical-research-toolbox/nimh-clinical-research-toolbox

University of Rochester Study Documentation Toolbox: https://www.rochester.edu/ohsp/quality/studyDocumentationToolBox.html

UC Davis Study Tools: https://health.ucdavis.edu/clinicaltrials/StudyTools/StudyTools.html

University of Wisconsin at Madison CRF Templates: Case Report Form Templates – ICTR – UW–Madison (wisc.edu)

UPitt GCP Toolbox: https://www.ecshsr.pitt.edu/monitoring-compliance/good-clinical-practice-gcp-toolbox

Breakout Room Activity

- We will use the breakout rooms to discuss our case. Each room will have a facilitator.
- Begin with discussing 2 of the lettered sections on the case (these will be assigned)
- Discuss the case…..
  - Think about the sources of the data (some from the EMR, some generated by study staff, etc.).
  - Consider your data management strategy: CRFs, data collection forms, what source is directly entered into the CRF vs. on a data collection form, etc.
  - Consider what data collection tools you need to develop to record the data.
  - Consider also how you will design your Case Report Forms (CFRs) and data collection tools
- We will have 25 minutes for the discussion.
- We will come back to the full group to discuss insights and learnings.